

CLAIMS

1. An electrode device comprising a nanotip wherein the nanotip comprises a diffusion barrier which restricts the movement of ions or molecules through an opening in the nanotip.
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2. The electrode device according to claim 2, wherein the electrode device comprises a housing defining a lumen for receiving an electrolyte solution and the diffusion barrier comprises a medium for lowering the diffusion of electrolytes in the electrolyte solution.
- 10 3. The electrode device according to claim 2, wherein the housing comprises an at least partially electrically conducting material.
4. The electrode device according to claim 1 or 2, wherein the housing comprises a contacting end for contacting biological molecules or macromolecules.
- 15 5. The electrode device according to claim 1 or 2, wherein the nanotip comprises a contacting end for contacting biological molecules or macromolecules and wherein the diameter of the contacting end is less than about 500 μm .
6. The electrode device according to claim 1 or 2, wherein the diameter of the contacting end is less than about 5 μm .
- 20 7. The electrode device according to claim 1 or 2, wherein the diameter of the contacting end is less than about 1 μm .
8. The electrode device according to claim 2, wherein the housing further comprises a seating end for receiving a solid conducting material.
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9. The electrode device according to claim 1, wherein the diffusion barrier is selected from the group consisting of a hydrogel, polycrylamide, agar, PEDOT, an ion resin exchange medium, glycerol, (poly-)ethylene glycol, ion shuttle

compound, , electrically conducting polymer, metal, and metal nanoparticle solutions.

10. The electrode device according to claim 9, wherein the ion resin exchange medium is Nafion®.
- 5 11. The electrode device according to claim 4, wherein the contacting end is tapered.
12. The electrode device according to claim 4, wherein the contacting end comprises an electrically conducting material.
13. An electrode device comprising a housing comprising a contacting end for contacting biological molecules or biological macromolecules and defining two
10 lumens comprising parallel longitudinal axes, each for receiving an electrically conducting medium.
14. The electrode device according to claim 13, wherein the electrically conducting medium in at least one lumen comprises a solid electrically conducting medium.
- 15 15. The electrode device according to claim 13 or 14, wherein the electrically conducting medium in at least one lumen comprises a liquid or semi-solid electrically conducting medium.
16. The electrode device according to claim 13, wherein contacting end is less than about 500 μm .
17. The electrode device according to claim 13, wherein the contacting end is less
20 than about 5 μm .
18. The electrode device according to claim 13, wherein the contacting end is less than about 1 μm .
19. The electrode device according to claim 13, wherein the contacting end is tapered.
20. The electrode device according to claim 13, wherein the contacting end comprises
25 an electrically conducting material.

21. The electrode device according to claim 13, further comprising a diffusion barrier.
22. The electrode device according to claim 13, wherein at least one lumen comprises a diffusion barrier.
23. The electrode device according to claim 13, wherein the device is capable of sequentially electroporating a cell or cell structure and recording electrical properties of the cell or cell structure.
24. A composite electrode comprising a housing comprising a contacting end for insertion into a cell and defining a lumen for containing an electrically conducting material, wherein the housing comprises a first and second layer of conducting material and wherein the first and the second layer are separated from each other by an insulating layer and wherein the contacting end is less than about 500 μm in diameter.
25. The composite electrode of claim 24, wherein the lumen comprises a liquid or semi-solid electrically conducting material.
26. The composite electrode of claim 24 or 25, wherein the lumen comprises a solid electrically conducting material.
27. The composite electrode of claim 24, wherein the contacting end is less than about 5 μm in diameter.
28. The composite electrode of claim 24, wherein the contacting end is less than about 1 μm in diameter.
29. The composite electrode of claim 24, wherein the contacting end is tapered to facilitate insertion into a cell.
30. The composite electrode of claim 24, wherein the contacting end comprises an electrically conducting material.
31. A nanoelectrode array comprising a plurality of electrodes devices according to any of claims 1, 2, 13 and 24. .

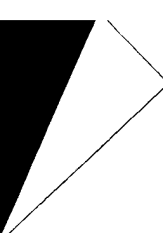
32. A substrate comprising a substantially planar solid material, wherein the material comprises a plurality of apertures and wherein the rims of the apertures are raised relative to the substantially planar solid material, and form electrically conducting tips for inserting into a cell or cell structure.
- 5 33. The substrate according to claim 32, wherein the conducting material is coated with an insulating material except at the tip of each aperture.
34. The substrate according to claim 32, wherein the aperture comprises a lumen for receiving a conducting medium.
- 10 35. The substrate according to claim 32, wherein the conducting medium is selected from the group consisting of a liquid conducting medium, a solid conducting medium, a semi-solid conducting medium and combinations thereof.
36. The substrate according to claim 32, wherein the medium is selected from the group consisting of an electrolyte solution, an electrically conducting polymer, a metal and a carbon fiber.
- 15 37. The substrate according to claim 32, wherein the substrate comprises a plurality of wells, each well comprising one of the apertures.
38. A plate comprising a substantially planar solid material, wherein the material comprises a plurality of solid electrode tips protruding from the material, each tip comprising a contacting end for insertion into a cell or cell structure.
- 20 39. The plate according to claim 38, wherein the tips are pins, wires, solid or hollow cylinders, or tubes.
40. The plate according to claim 38, wherein the contacting ends are tapered.
41. The plate according to claim 38, wherein the contacting end comprises an electrically conducting material.
- 25 42. The plate according to claim 38, wherein the contacting end of at least one tip is less than about 5 μm in diameter.
43. The plate according to claim 38, wherein the contacting end of at least one tip is less than about 1 μm in diameter.

44. The electrode device according to any of claims 4, 13 and 24, wherein at least a contacting surface of the device is hydrophilic.
45. The nanoelectrode array according to claim 31, wherein at least a contacting surface of the device is hydrophilic.
- 5 46. The substrate according to claim 32, wherein at least a contacting surface of at least one electrode tip is hydrophilic.
47. The plate according to claim 38, wherein at least a contacting surface of at least one electrode tip is hydrophilic.
48. The electrode device according to any of claims 4, 13 and 24, wherein at least a
10 contacting surface of the device is hydrophobic.
49. The nanoelectrode array according to claim 31, wherein at least a contacting surface of the device is hydrophobic.
50. The substrate according to claim 32, wherein at least a contacting surface of at least one electrode tip is hydrophobic.
- 15 51. The plate according to claim 38, wherein at least a contacting surface of at least one electrode tip is hydrophobic.
52. The nanoelectrode array according to claim 31, further comprising at least one microchannel in fluid communication with at least one electrode device.
53. The substrate according to claim 32, wherein the substrate comprises at least one
20 microchannel in fluid communication with at least one electrode device.
54. The plate according to claim 38, wherein the plate comprises at least one microchannel in fluid communication with at least one electrode tip.
55. A microfluidic system comprising a substrate, wherein the substrate comprises at least one measurement chamber comprising a substantially planar solid material,
25 wherein the material comprises at least one raised aperture, each aperture comprising a tip, and wherein the substrate further comprises at least one microchannel with an outlet which opens into the at least one measurement chamber.

56. The microfluidic system according to claim 55, wherein at least one of the at least one measurement chambers is circular and a plurality of microchannels are radially disposed about the chamber and comprise outlets that open into the chamber.
- 5 57. The microfluidic system according to claim 55, wherein the aperture comprises a lumen for receiving a conducting medium.
58. The microfluidic system according to claim 57, wherein the conducting medium is selected from the group consisting of a liquid conducting medium, a solid conducting medium, a semi-solid conducting medium and combinations thereof.
- 10 59. The microfluidic system according to claim 58, wherein the medium is selected from the group consisting of an electrolyte solution, an electrically conducting polymer, a metal and a carbon fiber.
60. A microfluidic system comprising a substrate, wherein the substrate comprises at least one measurement chamber comprising a substantially planar solid material, wherein the material comprises a plurality of solid electrode tips protruding from the material, and wherein the substrate further comprises at least one microchannel with an outlet which opens into the at least one measurement chamber.
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61. The system according to claim 55 or 60, wherein at least one tip is tapered to facilitate insertion into a cell or cell structure.
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62. The system according to claim 55 or 60, wherein at least one tip comprises a contacting surface for contacting biological molecules or macromolecules and wherein the contacting surface comprises a hydrophilic material.
63. The system according to claim 55 or 60, wherein at least one tip comprises a contacting surface for contacting biological molecules or macromolecules and wherein the contacting surface comprises a hydrophobic material.
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64. The system according to claim 62, wherein at least one contacting surface comprises a diameter of less than about 5 μm .

65. The system according to claim 62, wherein at least one contacting surface comprises a diameter of less than about 1 μm .
66. A system comprising a plate according to claim 38 and a microfluidic substrate comprising a plurality of measurement chambers wherein the location of tips on the plate corresponds to the location of measurement chambers in the microfluidic substrate such that bringing the plate in proximity to the microfluidic substrate brings the electrode tips in proximity to the measurement chambers in the substrate.
67. The system according to claim 55, 60 or 66, further comprising a pressure control device for controlling positive and negative pressure applied to at least one microchannel.
68. The nanoelectrode array according to claim 52, further a pressure control device for controlling positive and negative pressure applied to at least one microchannel.
69. The substrate according to claim 53, further comprising a pressure control device for controlling positive and negative pressure applied to at least one microchannel.
70. The plate according to claim 54, further comprising a pressure control device for controlling positive and negative pressure applied to at least one microchannel.
71. The system according to claim 55, 60 or 66, wherein the substrate is interfaced to a multiwell plate through one or more external tubings or capillaries.
72. The nanoelectrode array according to claim 52, wherein the array is interfaced to a multiwell plate through one or more external tubings or capillaries.
73. The substrate according to claim 53, wherein the substrate is interfaced to a multiwell plate through one or more external tubings or capillaries.
74. The plate according to claim 54, wherein the plate is interfaced to a multiwell plate through one or more external tubings or capillaries.

75. The system according to claim 55, 60 or 66, further comprising at least one cell or cell structure in the at least one measurement chamber.
76. The system according to claim 55, 60 or 66, wherein the system further comprises a scanning mechanism for scanning a cell or cell structure relative to a
5 microchannel outlet.
77. The system according to claim 55, wherein the system further comprises a scanning mechanism for scanning a cell or cell structure relative to an aperture of the system.
78. The system according to claim 60 or 65, wherein the system further comprises a
10 scanning mechanism for scanning a cell or cell structure relative to an electrode tip of the system.
79. The system according to claim 76, further comprising a processor in communication with the scanning mechanism.
80. The system according to claim 79, further comprising a processor in
15 communication with the scanning mechanism.
81. The system according to claim 80, wherein the processor controls one or more of: the rate of scanning, the direction of scanning, acceleration of scanning, and number of scans.
82. The system according to claim 81, wherein the processor controls one or more of
20 the rate of scanning, the direction of scanning, acceleration of scanning and number of scans.
83. The system according to claim 55, 60 or 66, further comprising an amplifier in communication with the at least one electrode.
84. The system according to claim 80, wherein in response to a signal from the
25 detector, the processor alters one or more of the rate of scanning, the direction of scanning, acceleration of scanning, and number of scans.

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85. The system according to claim 81, wherein in response to a signal from the detector, the processor alters one or more of the rate of scanning, the direction of scanning, acceleration of scanning, and number of scans.
- 5 86. The system according to claim 80, further comprising a user device in communication with the processor, the user device comprising a graphical user display for interfacing with a user.
87. The system according to claim 81, further comprising a user device in communication with the processor, the user device comprising a graphical user display for interfacing with a user.
- 10 88. The system according to claim 60 or 66, further comprising a plurality of microchannels, and wherein the microchannels deliver a plurality of substantially separate aqueous streams into the measurement chamber.
89. The system according to claim 88, further comprising a plurality of buffer delivery and agonist delivery channels, each channel comprising an outlet for
15 delivering a substantially separate aqueous stream into the chamber.
90. The system according to claim 88, further comprising a scanning mechanism for scanning a cell across the aqueous streams from the channels.
91. The system according to claim 88, wherein at least one microchannel delivers at least one agent into the measurement chamber.
- 20 92. A method for measuring an electrical property of a cell comprising bringing an electrode device according to claims 1, 2, 13 or 24 into proximity with the cell, inserting at least the tip of the device into the cell, and recording electrical properties of the cell with the electrode device.
93. The method according to claim 92, wherein the cell comprises an ion channel and
25 the electrical properties measured provide an indication of the activity of the ion channel.
94. The method according to claim 92, further comprising exposing the cell to a fluid stream and determining changes in the electrical properties of the cell in response to the exposing.

95. The method according to claim 94, wherein the fluid stream comprises a candidate therapeutic or toxic agent.
96. The method according to claim 93, further comprising exposing the cell to a fluid stream and determining changes in electrical properties of the cell in response to the exposing.
- 5 97. The method according to claim 96, further comprising exposing the cell to a candidate modulator of ion channel activity.
98. The method according to claim 97, further comprising determining a dose-response curve for the candidate modulator.
- 10 99. The method according to claim 92, further comprising electroporating the cell.
100. The method according to claim 99, further comprising introducing a cell-impermeable molecule into the cell.
101. The method according to claim 100, further comprising measuring an electrical property of the cell after the introducing.
- 15 102. The method according to claim 100, wherein the cell impermeable molecule is a pharmaceutical agent, a marker or a dye.